Hydrogel matrix to support stem cell survival after brain transplantation in stroke.

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Public Summary:
Stroke is a leading cause of adult disability. Stem/progenitor cell transplantation improves recovery after stroke in rodent models. These studies have 2 main limitations to clinical translation. First, most of the cells in stem/progenitor transplants die after brain transplantation. Second, intraparenchymal approaches target transplants to normal brain adjacent to the stroke, which is the site of the most extensive natural recovery in humans. Transplantation may damage this tissue. To look into the best strategy of cell transplantation, we test the area of the stroke cavity that can accept a high volume transplant without tissue damage. However, direct transplantation into the stroke cavity has caused massive death in the transplant. To overcome these limitations, we tested stem/progenitor transplants within a specific biopolymer hydrogel matrix to create a favorable environment for transplantation into the lesion cavity after stroke. A biopolymer hydrogel significantly promoted the survival of 2 different neural progenitor cell lines in vitro in conditions of stress and in vivo into the infarct cavity. This result indicates that altering the local environment in stem cell transplantation enhances survival and diminishes cell stress. Stem cell transplantation into the infarct cavity within a prosurvival hydrogel matrix may provide a translational therapy for stroke recovery.

Scientific Abstract:
Stroke is a leading cause of adult disability. Stem/progenitor cell transplantation improves recovery after stroke in rodent models. These studies have 2 main limitations to clinical translation. First, most of the cells in stem/progenitor transplants die after brain transplantation. Second, intraparenchymal approaches target transplants to normal brain adjacent to the stroke, which is the site of the most extensive natural recovery in humans. Transplantation may damage this tissue. The stroke cavity provides an ideal target for transplantation because it is a compartmentalized region of necrosis, can accept a high volume transplant without tissue damage, and lies directly adjacent to the most plastic brain area in stroke. However, direct transplantation into the stroke cavity has caused massive death in the transplant. To overcome these limitations, the authors tested stem/progenitor transplants within a specific biopolymer hydrogel matrix to create a favorable environment for transplantation into the infarct cavity after stroke, and they tested this in comparison to stem cell injection without hydrogel support. A biopolymer hydrogel composed of cross-linked hyaluronan and heparin sulfate significantly promoted the survival of 2 different neural progenitor cell lines in vitro in conditions of stress and in vivo into the infarct cavity. Quantitative analysis of the transplant and surrounding tissue indicates diminished inflammatory infiltration of the graft with the hydrogel transplant. This result indicates that altering the local environment in stem cell transplantation enhances survival and diminishes cell stress. Stem cell transplantation into the infarct cavity within a pro-survival hydrogel matrix may provide a translational therapy for stroke recovery.